REMARKS

Favorable reconsideration is respectfully requested in view of the following remarks.

Claims 5 and 6 were pending in this application when last examined and stand rejected.

On pages 3-5 of the Office Action, claims 5 and 6 were rejected under 35 U.S.C. 103(a) as obvious over Matsushima et al. in view of McColl et al. Applicants respectfully traverse this rejection.

Initially, it is again noted that the claimed invention is directed towards a transgenic rat with epileptic seizures during sleep. On the other hand, the cited references are directed towards mice. It is well known that native mice can have spontaneous seizures. However, native rats do show spontaneous seizures but have instead been used as models for drug induced seizures. Thus, a person of skill in the art would not have a reasonable expectation of success in creating a transgenic rat with spontaneous seizures during sleep. The Examiner is further again directed to Klaassen et al. (attached to the last response) directed towards a knock in mouse using a mutant CHRNA4 gene which is not shown to have spontaneous epileptic seizures. Furthermore, such reference is directed towards a knock in mouse which will only contain a mutant copy. On the other hand, as shown in the specification on pages 6 and 7, transgenic rats of the claimed invention may have a normal copy and a mutant copy of CHRNA4 and still have spontaneous seizures during sleep.

Thus, Applicants respectfully suggest that a person of skill in the art would not have a reasonable expectation of success in creating a spontaneous model of epileptic seizures during sleep using rats, as claimed in the claimed invention.

Furthermore, the Examiner states that "McColl teaches developing transgenic mice that are transgenic or knockout with respect to CHRNA4 mutations that are associated with ADNFLE (entire article, abstract)". The following is an excerpt from the Abstract of McColl et al.:

> *Mutant (Mt) and control mice underwent epidural electroencephalographic (EEG) recording for 2 h in the untreated state and for 1 h following administration of the y-amino butyric acid (GABA) antagonist, pentylenetetrazole (PTZ, 80 mg/kg). No spontaneous seizures occurred and no EEG differences were observed between the genotypes in drug naïve mice. Following PTZ, however, Mt mice showed markedly*

increased mortality compared to controls (85 vs. 30%, P<0.001). Mts also had a greater number of generalized clonic seizures in the first 40 min following injection. In the same period, the EEGs of Mt mice showed an excess of spikes (P=0.033), multi-spiky complexes (P=0.002) and continuous fast activity (P=0.017) compared to controls.

As you see, the mutant (transgenic) mice show no spontaneous seizures without PTZ. This is clearly different from the claimed rat, which develops a spontaneous epileptic seizure during sleep.

Thus, Applicants respectfully assert that one of skill in the art could not have a reasonable expectation of success for a transgenic mutant rat that develops a spontaneous epileptic seizure during sleep, from the teachings of McColl et al. either alone or in combination with Matsushima.

Thus, for the above noted reasons, this rejection is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

Shinichi HIROSE et al.

/William R. Schmidt, II/
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